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Keratosis Follicularis (Psorospermose
Folliculaire Végétante, Darier),
Apropos of a New Case.

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KERATOSIS FOLLICULARIS (PSOROSPERMOSE FOLLICULAIRE
VÉGÉTANTE, DARIER), APROPOS OF A NEW CASE.

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SINCE this interesting affection of the skin was first described almost simultaneously by Darier and White, an occasional instance has from time to time appeared in the literature, so that we are now in possession of the clinical history of about twenty cases, contributed by French, German, Norwegian, and American observers. It has been no surprise to find also that a considerable number of cases previously described under other headings were examples, in all probability, of this same dermatosis, although convincing histological proof is wanting. The publication of twenty cases within a period of seven years proves that the disease, although rare, occurs more frequently than some other affections, whose clinical features and pathological appearances have been for a long period described and studied. The interesting observation of Darier, that peculiar cell forms that resemble coccidiae are present in the cutaneous lesions, and his able exposition of the parasitic theory, have directed general attention to this subject on the part of those interested in skin affections, so that a larger number of cases have been recognized as examples of this affection than is usually the case when a group of symptoms is first accurately studied.

It was my fortune to observe and study at various times the two cases described by Dr. White, and to make an histological examination of numerous lesions and products of secretion and degeneration in both. At the time that the first case was published (JOURNAL OF CUTANEOUS AND GENITO-URINARY DISEASES, June, 1889), we had no knowledge of Darier's work, which had been communicated to the



Société de Biologie in March of that same year, but which first appeared in the *Annales de dermatologie et de syphiligraphie* of July. In this article Darier refers to White's case as probably identical in nature with his own, although the coccidia-like bodies had not attracted especial attention. An examination of a fresh and more abundant supply of material from this case, in the light of Darier's communication, proved that the peculiar cell forms existed in sufficient numbers, and that the disease was undoubtedly the same as that described by Darier. The affection had been called by White keratosis (ichthyosis) follicularis, as both the macroscopical and microscopical appearances suggested as the essential feature of the process a hyperkeratosis of the mouths of the hair and sebaceous follicles.

Soon after, a second case was published by White (*JOURNAL OF CUTANEOUS AND GENITO-URINARY DISEASES*, January, 1890), which afforded new material for the study of this interesting question, and my views with regard to the parasitic nature of the bodies in question were included in a report embodied in that article. Since then the subject has been of constant interest to me, and I have followed the series of reported cases with eagerness. In August, 1895, a fresh instance of the disease came into my hands, and, although the number of observations is rapidly reaching a point where a detailed description of single cases may appear unnecessary, I take the liberty, inasmuch as this is but the fourth case observed in America, of recording it in this place.

Case.—The patient was a woman twenty-nine years of age, living in a small city near Boston. Her father and mother were French Canadians, although she herself was born in the United States. No facts of importance in connection with the case could be obtained from her family history. She had no knowledge of the occurrence of any skin disease in any member of her family. One sister had died of phthisis two years previously. Two half-brothers and a half-sister were living and healthy. She had had an attack of diphtheria, and some "uterine troubles," but had been otherwise well, with the exception of the skin affection. She began to menstruate at the age of sixteen, and at this time, according to her own account, the skin of the face first became affected with the present trouble. Later, it spread downward gradually, but there had been no lesions upon the scalp until quite recently. There has been considerable itching, and she complains of a poor appetite and some debility.

The patient, when seen, presented the appearance of a fairly well nourished woman, of a dark, swarthy complexion. The face had an aspect quite characteristic of "Darier's dermatosis" to one who had

seen and studied the affection. It was covered with lesions that did not vary much in color from that of the normal skin, although there was a distinct darkening of the skin as a whole, which looked coarse, furrowed, and greasy.

On closer inspection it was seen that the individual lesions consisted of small, greasy-looking papules. They were, on an average, of about the size of a pin's head, although both larger and smaller examples were present. When closely examined it was found that the center of each papule contained a fatty-looking mass or plug. In some, the tip of the lesion showed a minute pustule instead of the greasy plug.

These lesions were apparent over the whole face. In certain regions, however, they were larger and more prominent. These regions were the forehead between the eyebrows, the cheeks near the alæ of the nose, and the temples near the line of the hair. In these situations, elevated areas had been formed by confluence of the individual nodules. These areas gave to the finger the sensation of a nutmeg grater. The surface of these elevated areas was uneven. Scattered over it were smaller or larger crateriform openings, filled with firm concretions. Large and somewhat confluent lesions were also present in front of the ears.

The ears were prominently affected. The external auditory canal was filled with lesions, showing a central orifice which contained a firm concretion. Some of these lesions had become confluent. The skin immediately behind the ears was the seat of very prominent, almost hemispherical, lesions, much larger and more rounded than those that have been described. Some of them exhibited no sign of a central opening; in others, a firm concretion occupied the center. These lesions were more or less confluent, so that the whole space behind the ear presented an irregular, papillomatous, fissured appearance.

The hair of the head had been cropped pretty closely, and the patient wore a wig. The hairs were dark, coarse, and vigorous. The scalp was covered with a thick mass of greasy concretions, closely aggregated, which, when removed, were found to dip down into shallow, crateriform depressions, surrounded by a slightly elevated rim. There were also numerous small pustules and excoriations.

Upon the trunk, the parts especially affected were the sternal, in terascapular, and sacral regions, and the median line of the abdomen from umbilicus to pubes. Here the lesions were numerous and closely aggregated. They were dark and greasy-looking, and less elevated than those on the face. Some of them bore a strong resemblance to *keratosis pilaris*.

The labia majora were the seat of prominent lesions, some of them the size of a large pea. By confluence of the individual lesions the labia had become much thickened, and precisely the same irregular papillomatous appearance was produced as has been described as occurring in the space behind the ears.

There were but a few scattered lesions upon the arms and legs, of small size. The hands and feet were perfectly free.

The finger nails were easily broken off, but were not otherwise deformed. The nails of the toes were normal.

Close inspection showed that the greater part of these lesions were grouped about the follicular orifices—in other words, that the affection was essentially a follicular one, at least at its inception. All the smaller, evidently primary lesions were seated about the follicles. In some places, however, as in the space behind the ears and on the labia majora, where large lesions had by their confluence formed fungous-looking, irregular, elevated areas, it was evident that the process had invaded the interfollicular structures to a considerable extent.

Under the influence of an ointment of sulphur and salicylic acid, together with daily washing, the scalp, as was to be expected, became much clearer, the pustular lesions and much of the concretion having been removed. The individual small papular elevations were thus brought out more prominently. The hypertrophied lesions behind the ear were also considerably diminished in size, and a marked improvement was noted everywhere except upon the body, to which it is probable the patient gave much less attention than to the exposed portions.

With regard to the histology of this case several lesions were excised and examined microscopically. I shall later consider the histological appearances of the three cases I have studied as a whole, and it need only be said here that this case corresponded perfectly with the others in its general pathological features, and in the presence of the cells that resemble coccidia. It will be noted that this case represented a lower grade of development than the first case reported by White and examined microscopically by me. In my case the process had not progressed to the formation of distinct horns, and the amount of epithelial proliferation at the edges of the nodules was far less, so that the papillomatous, tumorlike masses were only seen in the spaces behind the ear and on the labia. In grade of development it corresponded closely with the second of White's cases.

Before discussing the pathology of the disease, it may be of interest to examine the clinical characteristics, as shown by the twenty cases that have been reported. These are from the following sources:

Darier-Thibault (two cases),* White (two cases),† Boeck (five cases),‡ Buzzi and Miethke,§ Lustgarten,|| Schwimmer,^ De Amicis,◇ Schweninger and Buzzi,↓ Pawloff↓ (two cases), Fabry,‡ Mourek,** Jarisch,†† Bowen. The cases reported by Krösing, Manssuroff, and Zeleneff I have not considered. Krösing's case varies so essentially from the type of this disease that it should be placed aside for further study. Of Manssuroff and Zeleneff's cases I could find no sufficiently accurate description. Jarisch's differs more than any of the others from what we have now learned to be the clinical characteristics of this disease, but it is included on account of the histological appearances.

The age at which this affection begins seems to vary somewhat, so far as can be judged from the reported cases. It is probable, however, that it begins early in life, as in eleven out of the twenty cases the subjects testified that they were affected by or before the sixteenth year. In several it dated from early infancy. In all five of Boeck's cases it began between the eighth and the sixteenth year. It is extremely probable also that the testimony of the patients on this point is sometimes inaccurate, as an affection that is usually unaccompanied by subjective symptoms, and in which the primary lesions are insignificant, might very well excite little attention until fully developed. In some of the cases also there existed a motive which might induce the patient to declare the affection to be of later date than was true.

Of the twenty cases collected thirteen were males and seven females.

The portion of the body that was first affected is not mentioned in all the cases. In a considerable number, however, it was first noticed upon the head and face, extending afterward to the trunk and extremities.

It is to be noted that the affection belongs to the most obstinate of known dermatoses, as regards treatment. In most of the cases, especially in those where no care had been taken of the skin, a marked improvement has been effected. This is due to the removal of the semi-cornified and sebaceous masses in great degree, which in some instances,

* *Thèse de Paris*, 1889. *Annales de derm. et de syph.*, July, 1889.

† *JOURNAL OF CUT. AND GEN.-URIN. DIS.*, June, 1889, and January, 1890.

‡ *Archiv f. Derm. und Syph.*, 1891. Second International Congress of Derm. and Syph., Vienna, 1892.

§ *Monatsheft. f. prak. Derm.*, January, 1891.

|| *JOURNAL OF CUT. AND GEN.-URIN. DIS.*, 1891.

^ *Archiv f. Derm. und Syph.*, 1892.

◇ Vienna Congress, 1892.

↓ *Internation. Atlas seltener Hautkrankheiten*, 1892, ii.

↓ *Archiv f. Derm. und Syph.*, 1893.

‡ *Ibid.*, 1894.

** *Ibid.*, 1894.

†† *Ibid.*, 1895.

as in the first case reported by White, are intolerably offensive to the smell. No one, however, has been able to record a cure, as the condition returns rapidly when the treatment is intermitted. In this respect the disorder bears a closer resemblance to the anomalies of development, as ichthyosis, for example, than to the class of parasitic affections.

A point upon which there has been much diversity of opinion is whether the lesions are essentially follicular or not. Indeed, it is difficult to understand why there should be such a lack of unanimity in the observations in this respect. Darier, as is well known, proposed the name *psorospermose folliculaire végétante* for the affection, declaring, on the strength of the two cases studied by him, that the process was one affecting the hair and sebaceous follicles especially, although foci of disease were often found apart from these structures. The primary lesion is defined by Thibault, whom Darier quotes, as "*une petite papule surmontée d'une croûte d'un brun noirâtre ou grisâtre.*" White, whose first case was published before Darier's article had appeared, named the disease keratosis follicularis, and stated that at the beginning of the process we have lesions in no way to be distinguished from those of simple keratosis (lichen) pilaris. Lustgarten, an accomplished histologist, also concurred in the view that the lesions were essentially follicular. On the other hand, Boeck, in his admirable article based upon five cases, declares that he is unable to determine that the lesions are in great part confined to the follicles, although he admits that clinically as well as microscopically such an association is sometimes seen. Most of the remaining writers who have published single cases concur in this view.

In the face, therefore, of so much difference of opinion among experienced observers, it is difficult to speak categorically. For our own part we must adhere to our original position, which was taken at the time that we made the histological examination of White's first case, and before the studies of Darier had come to our notice, viz., that the process is primarily and essentially a keratosis of the mouths of the follicles. In the three cases seen in Boston, and repeatedly examined by both Dr. White and myself, no question existed in our minds that the follicles were primarily affected. This could be verified in every instance by the use of the hand lens. Through the courtesy of Dr. Lustgarten I had an opportunity of seeing and examining the case reported by him, and here too the follicular situation was evident to the naked eye. In all these cases the process had extended outside of the follicles also, as was seen especially in the confluent lesions behind the ears and in the groin.

Naturally, in the course of my studies of the two cases of White's

and of the one above reported, I have made an histological examination of a great many different lesions from the three cases. In no instance where the small primary greasy papule was excised have I failed to find the process situated about a hair or sebaceous follicle. It is very difficult to distinguish the smallest of these lesions from papules of keratosis (lichen) pilaris histologically, although a careful search will usually reveal traces of the perverted process of cornification which characterizes the disease. In larger lesions, especially the confluent masses from the groin and behind the ear, where there is a marked proliferation of the epithelium, the follicular origin is by no means always apparent. So far as the cases that I have examined are concerned, I must record myself emphatically on the side of Darier and Lustgarten, that the process is one affecting primarily and chiefly the mouths of the follicles, although it unquestionably appears also in their vicinity. It seems not improbable, from the varying testimony of those who have reported cases, that the disease may affect the follicles to a greater or less extent in different instances. Otherwise it is difficult to account for the diversity of opinion on this point.

With regard to the pathology of the disease, I insisted in 1889 that the lesions were caused by a hyperkeratosis that affected chiefly the sebaceous and hair follicles. This process does not extend far downward into the follicle, but is principally confined to the neck. The peculiar cell forms that have been described by Darier as parasites belonging to the coccidiæ were abundantly present in the three cases I have examined. At the time that I made the examination of White's first case Darier's work had not been published in the *Annales*, and these bodies did not attract especial attention, the amount of material examined being small. In the light of Darier's admirable and exhaustive work, they were readily found in a fresh and more abundant supply of material that was obtained from the first case, which was still under Dr. White's observation, and also in the second case reported by him. In a report that was published in connection with the latter case* I stated that I had been able to find them, but expressed my skepticism as to their parasitic nature, basing my doubts on the presence of eleidin and keratohyalin in their interior, and on the fact that their intracellular position could not be verified. It was also stated that in various other anomalies of cornification such bodies are occasionally seen, although never, so far as my experience extends, in such large numbers as in the disease we are dealing with. This has since been confirmed by Unna and others.

* JOURNAL OF CUTANEOUS AND GENITO-URINARY DISEASES, 1890.

With regard to the presence of keratohyalin in these cells, my observations have been confirmed by Buzzi and Miethke, Boeck, and by most of the writers who have published cases. This circumstance affords perhaps the strongest argument against their parasitic nature, as such an association does not occur in the case of any of the known coccidiæ.

The question whether Darier's "*corps ronds*" are inclosed in epithelial cells, as was claimed by him, is one that is not easily decided by an unprejudiced observer, studying for the first time the histology of this disease. At one period of my studies I was inclined to agree with Darier on this point, although I had previously expressed an opposite opinion. Since then repeated examinations of the horny material from these three cases have failed to convince me that the round bodies in question are contained in cells. Darier's conclusions on this point are drawn chiefly from the appearances seen in preparations made by softening the horny masses with dilute ammonia or potash and staining with hæmatoxylin. In such preparations we occasionally meet with appearances very similar to those depicted in Plate IV, Fig. 3, of Darier (*Annales de dermat. et de syph.*, 1889). The portion designated by *a*, which might be taken as the nucleus of the host cell pushed to one side by the parasite, is often, it seems to me, a part of the cell that has undergone an irregular cornification, and for this reason is differently affected by the staining agents from the rest of the cell. Certainly this explanation is a satisfactory one for many of the appearances seen by me in the so-called "squash" preparations. I have found it in these cases impossible to detect a distinct line of boundary between this supposed nucleus and the inclosed cell, and I am therefore inclined to regard the former as a part of the cell that has taken on a deeper stain than the remainder.

It seems to me that it is pretty well proved that the essential feature of the process is an irregular keratinization of the epidermal cells, a parakeratosis, as well as a hyperkeratosis, the formation of horny cells being effected in an irregular manner. Thus the "*corps ronds*" of Darier are epidermal cells that are enlarged and swollen, made up of a nucleus, with usually a clear or hyaline protoplasm around it (the kern-ring of Peterson),* and outside of this a zone containing granules of keratohyalin. Around and outside of this keratohyalin zone is the membrane so often referred to, that in some instances possesses a double contour (the mantel-ring of Peterson). This outer membrane is evidently an early cornified or hyaline structure, which is

* *Centralblatt für Bakteriologie u. Parasitenlehre*, October 16, 1893.

homogeneous and glistening and sharply bounded from the zone of keratohyalin. The keratohyalin zone gradually disappears in the upper more completely cornified layers, but this transformation is often accomplished in an irregular manner, so that at one portion of the zone a clump of keratohyalin which has partially lost its granular character may remain after the rest of the zone has become almost transparent. It is these clumps of partially transformed keratohyalin that produce the appearances in the "squash" preparations that at first sight impress one as the remains of nuclei. In sections no appearances are met with that simulate the nuclei of host cells.

The hyaline degenerated outer ring or membrane frequently becomes contracted or disappears in the upper layers of the rete and in the horny layers. In this way cell forms are often seen composed of nucleus surrounded by a ring of keratohyalin or partially cornified protoplasm; while, instead of the outer glistening double membrane, an empty space is observed. In other instances, the hyaline membrane is well seen in cells that are situated in the upper horny layers.

Another anomaly of cornification is found in these lesions. Many of the cells at the bottom of the follicle plugs become cornified without passing through the keratohyalin stage. Darier called attention at the outset to the frequent absence of the stratum granulosum at this point. These cell forms are rounded, sometimes polygonal, shrunken bodies, homogeneous, and with a feebly differentiated nucleus. These are the bodies that are seen in preparations obtained by macerating the horny plug, and to which Darier has given the name of "grains." It may be that some of the latter are formed from the "*corps ronds*," as it is certain, as Buzzi and Miethke have shown, that in some instances pretty direct transitional forms may be seen between the large round cells with hyaline glistening outer zone, and the compressed, homogeneous "grains." But the larger portion of the "grains" found in the horny plug, I think with Peterson and Unna, are epithelial cells that have become cornified without passing through the keratohyalin stage, and such as are seen loosely clustered, and not bound together, in the lowest rete layers. In the cases where a firm horn is produced, as occurred in the first case of White's, the horny plug is made up at its outer part of bands of horny fibers, running vertically and obliquely and without trace of the "grains." The outer portion of these horns, which were apparently more developed than in any other case yet published, differed therefore in no respect histologically from the ordinary cutaneous horn.

Boeck first called attention to the presence of fissures or lacunæ in

the lower layers of the rete. Buzzi and Miethke believe that these lacunæ are the result of an exudative process and are analogous to bullæ, since threads of fibrin and lymphoid cells have been found in them. I do not share this view, but believe with Boeck that they are caused by fracture occurring between the soft, pliable cells of the lowest rete and the hard, precociously cornified cells immediately above. This view is supported by the fact that similar fractures may be seen in other forms of hyperkeratosis, and that the appearances are not constant in this disease.

In the epidermis and corium at the borders of the lesions there is usually an abundant deposit of pigment. The amount of cellular infiltration in the corium is very small, and there can be no question that the affection is primarily and essentially a disease of the epidermis. The proliferation of the rete into the corium, which often produces tumorlike masses in the groin and behind the ears, has been recognized by all observers, and is undoubtedly secondary to the keratosis. In the primary, follicular lesion, which is still very small, this epithelial proliferation is not seen. No instance has yet been recorded where this epithelial activity took on a malignant character; but it would not be strange if such were exceptionally the case, in view of the fact that in other examples of keratosis such a change is sometimes observed.

It is not out of place to call attention, in conclusion, to the fact that at the time White's first case was published in 1889, and before Darier's interesting article had appeared in the *Annales*, the affection was regarded and described as a keratosis affecting primarily the follicles. With regard to this, his first case, that had reached a far higher grade of development than most of the cases since reported, White * says: "It is easy to trace the intimate connection between the various lesions by their progressive development from the minute primary papule to the largest masses of hornlike concretion. At the beginning of the process we have lesions in no way to be distinguished from those of simple keratosis (*lichen*) *pilaris*, while the other extreme is characterized by formations resembling well-marked *ichtyosis cornea*. The disease is, then, evidently in all its phases a keratosis, or primarily a hypertrophy, or modified cornification of the epithelial layers. It is also evident that its starting point is in or about the follicular openings." This view was supported by the microscopical examination that I made at the time, which proved to me conclusively that we had to do with a keratosis of the neck of the follicles.

* JOURNAL OF CUT. AND GEN.-URIN. DIS., June, 1889.

When White's second case * was published, I expressed, as has been said, in a report incorporated in that paper, my skepticism as to the parasitic nature of the cell forms described by Darier, pointed out that the presence of keratohyalin and eleidin in their interior was inconsistent with the view that they were coccidia, and again insisted upon the anomalies of cornification that characterized the process.

This repeated reference to the years 1889 and 1890 has its justification in the fact that the later writers, with the exception of Boeck and Buzzi and Miethke, have approached the subject solely from the standpoint of Darier's article, and, while ignoring the work embodied in the reports of White's two cases, have finally arrived at conclusions that do not differ from the latter's as to the essential nature of the process.

The adjective follicularis may not seem appropriate to those observers who have failed to recognize the follicles as the chief and primary seat of the morbid process. As has been said, our own observations point to these structures as the parts chiefly and primarily involved, although we freely admit, with Darier and Lustgarten, that the process is not confined wholly to them, but is found also in their neighborhood.

Credit is due to M. Darier, who has done so much, by his description of the "*corps ronds*" and "*grains*," toward the general recognition of this interesting dermatosis. The brilliant and attractive theory that these cells represent parasites of the order sporozoa has not stood the test of time. With the abandonment of this theory and of the assumption that a great part of the concretions is made up of these parasites, we can no longer doubt that the view taken by White in 1889, from the clinical appearances, and confirmed by microscopical studies made by me, is essentially the correct one; viz., that "the disease is evidently in all its phases a keratosis or modified cornification of the epithelial layers." Both clinically and histologically it appears to resemble the anomalies of development, as exemplified by ichthyosis, more closely than any other group.

* JOURNAL OF CUT. AND GEN.-URIN. DIS., January, 1890.

